UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,515	10/06/2005	Ira Pastan	4239-68223-02	1944

36218 7590 01/30/2008
KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET
SUITE #1600
PORTLAND, OR 97204-2988

EXAMINER	
GODDARD, LAURA B	
ART UNIT	**PAPER NUMBER**
1642	

MAIL DATE	DELIVERY MODE
01/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,515	PASTAN ET AL.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-53* is/are pending in the application.

4a) Of the above claim(s) *12-23,31-38 and 41-46* is/are withdrawn from consideration.

5)☒ Claim(s) *7-9* is/are allowed.

6)☒ Claim(s) *1, 4-6, 10, 11, 24-30, 39, 40, and 47-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 April 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendments filed March 5, 2007, July 30, 2007, and October 30, 2007 in response to the Office Action of November 29, 2006, are acknowledged and have been entered.

Claims 1 and 4-53 are pending. New claims 49-53 were added. Claims 2 and 3 are canceled. Previously pending claims 7, 8, 9, 10, 24, 25, and 40 have been amended. Claims 12-23, 31-38, and 41-46 remain withdrawn. Previously withdrawn method claims 24 and 25 are hereby rejoined for examination in view of their dependence on allowed product claim 7. Claims 1, 4-11, 24-30, 39, 40, and 47-53 are currently being examined.

Rejections Maintained

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. **Claims 1, 4, 5, 39, 47, and 48 remain rejected under 35 U.S.C. 101** because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility (see section 4 of the previous Office Action).

The claims are drawn to an isolated polypeptide comprising: (1) at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule; or (2) an

amino acid sequence set forth as SEQ ID NO:1 (claim 1), the isolated polypeptide of claim 1 comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule (claim 4), the isolated polypeptide of claim 1, comprising an amino acid sequence as set forth as SEQ ID NO:1 (claim 5), a pharmaceutical composition comprising a therapeutically effective amount of the polypeptide of claim 1 in a pharmaceutically acceptable carrier (claim 39), the isolated polypeptide of claim 1 consisting of at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule (claim 47), a fusion protein comprising (a) the polypeptide of claim 1, wherein the polypeptide consists of at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is at least eight to ten amino acids in length and binds a MHC molecule; and (b) a heterologous polypeptide (claim 48).

The specification discloses a predicted amino acid sequence for an SV-NGEP protein based on the nucleotide sequence of SEQ ID NO:2 (p 51, lines 18-21; Example 3). SEQ ID NO:2, the polynucleotide, was found to be uniquely expressed in prostate tissue and prostate cancer tissue but not in other normal tissues (Example 2). The specification discloses the prediction of 9-mers of SEQ ID NO:1 that would bind to HLA2-01 (an MHC molecule) (p. 25, lines 12-26). The specification does not provide any working examples with regards to the function or use of the disclosed SV-NGEP protein.

The specification prophetically asserts a specific utility for the claimed polypeptides in methods of producing an antibody for the detection of the claimed polypeptide in order to detect prostate tissue (p. 31, 46-47; Example 8), administering a SV-NGEP polypeptide to a subject to generate an immune response (p. 39), administering a SV-NGEP polypeptide to induce a CTL response (p. 40; Example 9). It is noted that the specification lacks working models demonstrating all of these utilities.

Following the requirements of the Utility Guidelines, (<http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf>), "substantial utility" is a utility that defines "real world use", wherein utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant case, the asserted "real world" utilities of the claimed polypeptides are producing an antibody for the detection of the claimed polypeptide in order to detect prostate tissue, administering a SV-NGEP polypeptide to a subject to generate an immune response, administering a SV-NGEP polypeptide to induce a CTL response. These asserted "real world" utilities are not supported by the specification or the prior art. The specification neither identifies the functions of the proteins, nor demonstrates that the claimed proteins are associated with any diseases or would predictably treat any disease.

The state of the prior art does not appear to teach the claimed polypeptides.

Utility must be in readily available form. One of skill in the art would recognize that novel biological molecules, such as the claimed polypeptides, lack an established utility and must undergo extensive experimentation to determine an appropriate specific,

substantial, and credible utility. It is possible that, after further characterization, the claimed polypeptides might be found to have patentable utility. This further characterization, however, is part of the act of the invention, and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility.

The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where *specific* benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to polypeptides with undetermined function or biological significance. Until a specific real world utility is attributed to the claimed polypeptides, the claimed invention is incomplete. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for

the disclosed polypeptides. Because the claimed invention is not supported by a specific and substantial utility for the reasons set forth, credibility of any utility cannot be assessed.

Response to Arguments

3. Applicants state that as noted in the Office Action, the specification describes the use of the claimed polypeptides to (1) produce an antibody to detect prostate cells, (2) administer the polypeptide to a subject to generate an immune response, (3) administer the polypeptide to induce a cytotoxic T cell response. Applicants argue that all of these utilities are specific, substantial and credible. Applicants cite MPEP 2107.02 regarding proper rejection under 35 USC 101. Applicants argue that the Office Action provides no factual basis that would lead one skilled in the art to question the asserted utilities and argue the utility rejection should be withdrawn (p. 11-12).

The arguments have been considered but are not found persuasive. MPEP 2107.02 states:

> To properly reject a claimed invention under 35 U.S.C. 101, the Office must (A) make a prima facie showing that the claimed invention lacks utility, and (B) provide a sufficient evidentiary basis for factual assumptions relied upon in establishing the prima facie showing.
>
> The prima facie showing must be set forth in a well-reasoned statement. Any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility. Whenever possible, the examiner should provide documentary evidence regardless of publication date (e.g., scientific or technical journals, excerpts from treatises or books, or U.S. or foreign patents) to support the factual basis for the prima facie showing of no specific and substantial credible utility. **If documentary evidence is not available, the examiner should specifically explain the scientific basis for his or her factual conclusions.**
>
> Where the asserted utility is not specific or substantial, a prima facie showing must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The prima facie showing must contain the following elements:

(A) An explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is neither both specific and substantial nor well-established;
(B) Support for factual findings relied upon in reaching this conclusion; and
(C) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

Examiner has explained the factual basis that would lead one skilled in the art to question the asserted utilities. The scientific and factual basis for Examiner's conclusion is clearly stated in the rejection above: "The specification prophetically asserts a specific utility for the claimed polypeptides in methods of producing an antibody for the detection of the claimed polypeptide in order to detect prostate tissue (p. 31, 46-47; Example 8), administering a SV-NGEP polypeptide to a subject to generate an immune response (p. 39), administering a SV-NGEP polypeptide to induce a CTL response (p. 40; Example 9). It is noted that the specification lacks working models demonstrating all of these utilities.

Following the requirements of the Utility Guidelines, (<http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf>), "substantial utility" is a utility that defines "real world use", wherein utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant case, the asserted "real world" utilities of the claimed polypeptides are producing an antibody for the detection of the claimed polypeptide in order to detect prostate tissue, administering a SV-NGEP polypeptide to a subject to generate an immune response, administering a SV-NGEP polypeptide to induce a CTL response. These asserted "real world" utilities are not supported by the specification or the prior art. The specification neither identifies the functions of the proteins, nor

demonstrates that the claimed proteins are associated with any diseases or would predictably treat any disease.

The state of the prior art does not appear to teach the claimed polypeptides."

Examiner provided a scientific and factual basis for determining lack of utility for the asserted utilities. Neither the specification nor the prior art have provided any evidence that the claimed protein is differentially expressed, hence there is no specific utility for the claimed protein. Any protein that is expressed in prostate tissues shares the property of being able to be used to detect prostate tissues, and this is not a use that relies on any specific property of the claimed protein. Further, research needed to determine what the protein does in order to determine what to use it for is not substantial utility because it requires further experimentation.

As stated in the previous Office Action: "Utility must be in readily available form. One of skill in the art would recognize that novel biological molecules, such as the claimed polypeptides, lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility. It is possible that, after further characterization, the claimed polypeptides might be found to have patentable utility. This further characterization, however, is part of the act of the invention, and until it has been undertaken, Applicant's claimed invention is incomplete".

4. Applicants submit an article by Das et al, published in 2007, and argue that it rebuts the prima facie case for lack of utility because it describes the production of antibodies to NGEP using methods described in the specification on page 31, line 28 to

page 37, line 29. Applicants argue these antibodies were used to detect NGEP in protein extracts of prostate and prostate cancer. Applicants argue that the claimed polypeptides were demonstrated to have "real world" utility of producing antibodies that detect prostate cells, such as for histological evaluation as described in the specification (p. 12-13).

The arguments have been carefully considered but are not persuasive. As stated by Examiner above, neither the specification nor the prior art have provided any evidence that the claimed protein is differentially expressed, hence there is no specific utility for the claimed protein. Any protein that is expressed in prostate tissues shares the property of being able to be used to detect prostate tissues, and this is not a use that relies on any specific property of the claimed protein. Further, research needed to determine what the protein does in order to determine what to use it for is not substantial utility because it requires further experimentation.

With regards to the Das et al 2007 publication, published two years after the filing date and 4 years after the priority date of the instant application, the post-file publication does not demonstrate that utility was specific and substantial with regards to detecting prostate tissue for the reasons set forth above, nor does it demonstrate that utility was well-established **at the time of filing**. MPEP 2107 states that Applicant can:

> (ii) Provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. The examiner should review any subsequently submitted evidence of utility using the criteria outlined above. The examiner should also ensure that there is an adequate nexus between the evidence and the properties of the now claimed subject matter as disclosed in the application as filed. That is, the applicant has the burden to establish a probative relation

between the submitted evidence and the originally disclosed properties of the claimed invention.

Applicants have not provided persuasive evidence that the asserted utilities are specific, substantial, or well-established at the time of filing.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. **Claims 1, 4, 5, 26-30, 39, 47, and 48 remain rejected under 35 U.S.C. 112, first paragraph.** Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know *how to use* the claimed invention (see section 5 of the previous Office Action).

Response to Arguments

6. Applicants argue that there is at least one specific, substantial and credible utility set forth in the specification (as argued above). Applicants argue the Das et al article submitted documents the use of the claimed polypeptides to produce antibodies that specifically bind prostate tissue cells and prostate cancer cells (as argued above). Applicants summarize disclosures in the specification related to polypeptides SEQ ID NO:1 and fragments of SEQ ID NO:1 that are at least 8 amino acids in length that can

be used to produce antibodies or to bind MHC. Applicants summarize the disclosures in the specification related to the asserted utility for the claimed polypeptides to produce antibodies for Western blots and to detect prostate cells. Applicants argue these disclosures from the specification provide more than adequate guidance for one of skill in the art to use the claimed polypeptides and this assertion is supported by Das et al. Applicants argue that Das et al provides documentary evidence that one of skill in the art could readily make and use the claimed polypeptides given the guidance in the specification (p. 13-14).

The arguments have been considered and are not found persuasive. Examiner maintains that the asserted utilities for claimed proteins are not specific, substantial, or well-established for the reasons set forth above. Examiner maintains that the Das et al article is not persuasive for the reasons set forth above. Further, MPEP 2164.05 states:

> Applicant may submit factual affidavits under 37 CFR 1.132 or cite references to show what one skilled in the art knew **at the time of filing the application.**
>
> The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling **as of the filing date.**
>
> Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known **at the time of filing**.

The post-file published Das et al article does not provide evidence that the instant invention has specific, substantial, or well-established utility nor that the invention was enabled at the time of filing.

Claims 1, 4, 5, 26-30, 39, 47, and 48 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record.

7. **Claims 6 and 40 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection (see precious Office Action section 6).

The claims are drawn to an isolated nucleic acid sequence encoding the polypeptide of claim 1, wherein the polypeptide of claim 1 comprises: (1) at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule (claim 6), and a composition comprising a therapeutically effective amount of the polynucleotide of claim 6 (claim 40).

The specification discloses SV-NGEP sequence SEQ ID NO:2 which was detected as a gene uniquely expressed in prostate tissue (Fig. 3; Examples 2 and 3). The specification does not disclose any other nucleic acids that encode a polypeptide comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule as broadly encompassed in the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because

> it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed

correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus, the instant specification may provide an adequate written description nucleic acids that encode a polypeptide comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule, per Lilly by structurally describing representative nucleic acids that encode a polypeptide comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe nucleic acids that encode a polypeptide comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule useful in the claimed invention in a manner that satisfies

either the Lilly or Enzo standards. Although the specification discloses SEQ ID NO:2 which is predicted to encode SEQ ID NO:1, this does not provide a description of the broadly claimed nucleic acids that encode a polypeptide comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule that would satisfy the standard set out in Enzo because the specification provides no structural features coupled to the functional characteristics.

Further, the specification also fails to describe nucleic acids that encode a polypeptide comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule by the test set out in Lilly because the specification describes only SEQ ID NO:2. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of nucleic acids that encode a polypeptide comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule that is required to practice the claimed invention.

Response to Arguments

8. Applicants argue adequate written description for polynucleotides encoding the polypeptide sequence set forth as SEQ ID NO:1 (claim 1, part a) on pages 14-15 of the

Remarks, however Examiner never rejected these specific polynucleotides, therefore the arguments are moot.

9. Applicants argue that there is sufficient written description for a polynucleotide encoding a polypeptide comprising eight to ten consecutive amino acids of SEQ ID NO:1. Applicants argue that the specification describes several polypeptides of eight to ten consecutive amino acids of SEQ ID NO:1 (see for example, page 24, line 1 to page, line 14). Applicants argue that eight specific polypeptide sequences (SEQ ID NOs:3-10) are provided that are nine consecutive amino acids in length of SEQ ID NO:1. The HLA binding motif program (available for free use on the internet) confirms that these eight polypeptides will bind MHC (see the specification at page 25, lines 12-24).

The arguments have been considered but are not found persuasive. The claims are drawn to a broad genus of polynucleotides encoding a polypeptide comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the polypeptide is eight to ten amino acids in length and binds an MHC molecule. The specification discloses examples of peptide sequences derived from SEQ ID NO:1 (SEQ ID NOs:3-10) that are predicted to bind to MHC by a computer program (an HLA binding motif program). The specification discloses that "additional epitopes of interest can be identified using computer programs available on the internet" (p. 25, lines 24-26). The specification and claims do not identify which structural features are conserved among the polypeptides encoded by the claimed polynucleotides, or which structures constitute a substantial portion of the genus in order for one to visualize or recognize

the identity of the members of the genus, hence the written description for the broad genus of polynucleotides in the claimed methods do not meet the standards of Lilly. Screening assays, such as computer programs, are merely a wish or plan for obtaining the claimed invention that has not been adequately described by the specification. Neither the claims nor the specification teach the amino acids critical to the function, *i.e.*-binds to an MHC molecule, of any polypeptide encoded by the claimed polynucleotides. Although the specification discloses specific SEQ ID NOs of polypeptides predicted by a computer program to bind an MHC molecule, neither the claims nor the specification teach the amino acids critical to the function, *i.e.*-binding an MHC molecule, of the broad genus of polypeptides encoded by the claimed polynucleotides, hence the specification does not provide adequate written description according to the standards of Enzo.

10. **Claim 6 remains rejected and new claims 49-51 are rejected under 35 U.S.C. 112, first paragraph**, because the specification, while being enabling for **an isolated nucleic acid sequence encoding the polypeptide SEQ ID NO:1**, does not reasonably provide enablement for a polynucleotide encoding a polypeptide comprising or a polypeptide consisting of at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds a MHC molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

practice the invention commensurate in scope with these claims (see section 7 of the previous Office Action).

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to an isolated nucleic acid sequence encoding a polypeptide comprising or a polypeptide consisting of at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1, wherein the isolated polypeptide is eight to ten amino acids in length and binds an MHC molecule.

The specification discloses polynucleotide SEQ ID NO:2, SV-NGEP, was found

to be uniquely expressed in prostate tissue and prostate cancer tissue but not in other normal tissues (Example 2). The specification discloses methods of detecting SEQ ID NO:2 to detect SV-NGEP expressing prostate cells in samples (p. 46, lines 30-33; p. 48, lines 10-30; Example 2).

One cannot extrapolate the disclosure of the specification to the enablement of the claims because the specification does not provide guidance or examples for making and using polynucleotides that would encode the broadly claimed polypeptides that would function to bind an MHC molecule. The specification discloses only polynucleotide SEQ ID NO:2, which is uniquely expressed in prostate tissue and can be used as a marker for prostate tissue. A search of the art does not appear to enable the use of any other polynucleotides that encode the claimed polypeptides. Given the lack of utility and enablement for the claimed polypeptides as stated in the rejections of sections 4 and 5 of the previous Office Action, one of skill in the art would not know how to use the polynucleotides encoding a polypeptide comprising or a polypeptide consisting of at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1; wherein the isolated polypeptide is eight to ten amino acids in length and binds an MHC molecule.

The specification discloses that the claimed polynucleotides are novel (p. 5, lines 1-4). It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that

information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Bera et al (PNAS, 2004, 101:3059-3064) teach SEQ ID NO:2 as a long form splice variant of "Novel Gene Expressed in Prostate" (NGEP-L) which is expressed only in prostate tissue (p. 3061, col. 2), however, a search of the art does not appear to enable the use of any other polynucleotides encoding the claimed polypeptides as contemplated by the specification. MPEP 2164.03 states: The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. One of skill in the art would not know how to use the claimed polynucleotides, other than SEQ ID NO:2, to predictably function as claimed and contemplated.

Therefore, in view of the novel nature of the invention, what is unknown in the art because of the novel nature of the invention, the breadth of the claims, lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Response to Arguments

11. With regards to the Wands factors in determining whether undue experimentation is required, Applicants argue: (1) the scope of the claims is limited to fragments of a specified length of a single amino acid sequence that can bind MHC class I and these fragments must include contiguous amino acids; (2) the invention is limited to polypeptides that consist of 8 to 10 consecutive amino acids of amino acids 157-933 of SEQ ID NO:1 that bind MHC class I; (3) the prior art teaches how to identify epitopes of a specified protein sequence that will bind MHC and induce an immune response; computer programs were available at the time of filing wherein a technician can enter a specified amino acid sequence and the computer will predict which amino acid segment will bind MHC, such as HLA-A2; to identify polypeptides consisting of eight to ten amino acids in length that bind MHC, the NGEP amino acid sequence can be entered into a computer program to identify epitopes of interest and programs were publicly available for identification of epitopes that bind MHC and known to those of skill in the art at the time of filing; the production of nucleic acids encoding a specified amino acid sequence is well known in the art, and described in the specification;(4) the level of skill of the average molecular biologist is high; (5) computer programs can be used to predict

which eight to ten consecutive amino acids of a specified polypeptide are likely to bind MHC, once polypeptides are identified, a biological assay can be used to confirm that the eight to ten consecutive amino acids actually bind MHC; the generation of peptide specific cells is known in the art and the production of nucleic acids encoding a specified polypeptide is routine, using materials such as expression vectors and host cells that are publicly available; (6) there is considerable direction provided in the specification including the amino acid sequence of NGEP is provided (SEQ ID NO:1), immunogenic peptides are described in the specification, exemplary peptides are disclosed, and methods for the production of polynucleotides encoding these polypeptides are described in detail; (7) the specification describes eight 9-mers of SEQ ID NO:1 that bind MHC; with regards to *In re Bundy*, appellant's disclosure was sufficient to enable one skilled in the art to use the claimed analogs of naturally occurring prostoglandins even though the specification lacked any examples of specific dosages, because the specification taught that the novel prostoglandins had certain pharmacological properties and possessed activity similar to known E-type prostoglandins; Applicants argue this is similar to the present application, wherein the specification teaches that the novel peptides have specific pharmacological properties and possess a specified activity (the binding of MHC); Applicants further argue the specific physical properties of the claimed polypeptides are disclosed (the presence of anchor residues) and the production of a fragment of NGEP is described in the specification; (8) once a polypeptide consisting of eight to ten consecutive amino acids of SEQ DI NO:1 is identified using an art-recognized program, polynucleotides encoding

the polypeptide can readily be produced using standard methods in molecular biology; thus only very limited routing experimentation is required to produce the claimed polynucleotides; this given the very complete disclosure provided by the specification, only limited experimentation is required.

The arguments have been carefully considered but are not found persuasive. The lack of utility and enablement for the claimed polypeptides were addressed above. As stated in the rejection above, "Given the lack of utility and enablement for the claimed polypeptides as stated in the rejections of sections 4 and 5 of the previous Office Action, one of skill in the art would not know how to use the polynucleotides encoding a polypeptide comprising or a polypeptide consisting of at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO:1; wherein the isolated polypeptide is eight to ten amino acids in length and binds an MHC molecule".

(1) and (2): Although Applicants argue the claims are limited in scope and the nature of the invention is limited to polypeptides that consist of 8 to 10 consecutive amino acids from amino acids 157-933 of SEQ ID NO:1 that bind to MHC class I, these claimed polypeptides lack utility and enablement for the reasons of record, therefore the polynucleotides encoding them lack enablement for the reasons of record.

(3): Although Applicants argue computer programs were available and well known at the time of filing for identifying epitopes in SEQ ID NO:1 for binding to MHC molecules, the claimed polypeptides, including any peptides from SEQ ID NO:1 further identified by known computer programs, are not enabled and do not have utility for the reasons of record, therefore the polynucleotides encoding them lack enablement for the

reasons of record.

(4) and (5): Although Applicants argue that computer programs can be used to predict which eight to ten consecutive amino acids of a specified polypeptide are likely to bind MHC and Applicants admit that further testing is required to determine if these peptides actually bind MHC, the claimed polypeptides identified by such computer programs lack utility and enablement for the reasons of record and the polynucleotides encoding these polypeptides lack enablement for the reasons of record. The skill level of a molecular biologist is high.

(6): Although the specification discloses SEQ ID NO:1 and exemplary peptides from SEQ ID NO:1 that are predicted by a computer program to bind MHC, the claimed polypeptides identified by such computer programs lack utility and enablement for the reasons of record and the polynucleotides encoding these polypeptides lack enablement for the reasons of record.

(7): Applicants appear to argue that the disclosure of peptides from SEQ ID NO:1 that are predicted by a computer program to bind MHC constitute a working example. As stated previously, the specification does not provide any working examples with regards to the function or use of the disclosed SV-NGEP protein or computer-identified MHC epitopes and asserts prophetic utilities for the claimed proteins. The decision and fact pattern in *In re Bundy* is not commensurate in scope with the claimed polynucleotides encoding the claimed polypeptides. Unlike in *In re Bundy*, the art does not teach structurally and functionally similar proteins or peptides to those claimed in the instant application and a search of the art does not appear to enable the use of the

claimed polypeptides, hence the polynucleotides encoding these polypeptides lack enablement for the reasons of record. One of skill in the art would not reasonably extrapolate the enablement of MHC-binding peptides derived from unrelated proteins to the enablement of the unrelated claimed peptides. Further, the specification and Applicants do not teach any enabled proteins or peptides structurally and functionally similar to SEQ ID NO:1 and its predicted MHC binding peptides, therefore the polynucleotides encoding the claimed polypeptides are not enabled for the reasons of record.

(8): Although Applicants argue limited experimentation is required to identify MHC binding peptides of SEQ ID NO:1 using known computer programs, as well as making polynucleotides to encode them, given the lack of utility and enablement for the claimed polypeptides for the reasons of record, the quantity of experimentation required to make and use the claimed polynucleotides encoding these polypeptides as contemplated is high.

12. **Claims 10, 11, and 40 remain rejected and new claims 52 and 53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (see section 8 of the previous Office Action).

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are now drawn to a **host cell** transfected with the nucleic acid of claim 7 or claim 50 (claim 10 and 52, respectively), wherein the host cell is a mammalian cell (claims 11 and 53), a composition comprising a therapeutically effective amount of the polynucleotide of claim 6 (claim 40).

It is noted that claims 10, 11, 52 and 53 reasonably read on the transfection of intact hosts and mammalian hosts with the claimed vector, and amended claim 40 still reasonably reads on a therapeutic or pharmaceutical composition.

The specification contemplates administering SV-NGEP polynucleotides to elicit an immune response or immunize mammals (p. 42, lines 16-20; p. 43, lines 5-21) for therapeutic purposes such as therapy for prostate cancer (p. 44, lines 22-24; Example 7).

One cannot extrapolate the disclosure of the specification to the enablement of the claims because the specification does not provide guidance or examples for the claimed polynucleotides functioning as a therapeutic. One cannot extrapolate the disclosure of the specification to the enablement of the claims because the specification does not provide guidance or examples for transfecting an intact mammal or host with the claimed polynucleotides wherein the polynucleotides would function in immunizing or therapy of mammals for cancer as contemplated by the specification. A search of the art does not appear to teach and enable the claimed polynucleotides to predictably function therapeutically or for the transfection of hosts for the purposes of immunization or therapy.

The specification discloses that the claimed polynucleotides are novel (p. 5, lines 1-4). It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art

is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Therefore, in view of the novel nature of the invention, what is unknown in the art because of the novel nature of the invention, the breadth of the claims, lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Amendment of claims 10 and 52 to recite "an **isolated** host cell" would obviate this rejection of claims 10, 11, 52, and 53.

Response to Arguments

13. Applicants did not specifically address the arguments drawn to lack of enablement for a host cell transfected with the claimed nucleic acids or enablement for therapeutic properties of the claimed polynucleotides. Because Applicants presented no reasons why this rejection was improper, the rejection is maintained.

New Rejection

(necessitated by amendments and rejoinder)

Claim Rejections - 35 USC § 112

14. Claims 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method for detecting prostate cancer in a subject, comprising detecting expression of the polynucleotide of claim 7 in a sample from the subject, wherein an increase in the expression of the polynucleotide as compared to a control indicates the presence of the prostate cancer (claim 24), wherein detecting the

expression of the polynucleotide comprises detecting mRNA in a Northern Blot analysis, an RNA Dot blot, or an RT-PCR assay (claim 25).

The specification discloses SV-NGEP sequence SEQ ID NO:2 which was detected as a gene uniquely expressed in normal prostate tissue (Fig. 3; Examples 2 and 3). The specification discloses that SEQ ID NO:2 is also expressed in prostate cancer samples (Example 5).

Bera et al (PNAS, 2004, 101:3059-3064) teach SEQ ID NO:2 as a long form splice variant of "Novel Gene Expressed in Prostate" (NGEP-L) which is expressed only in prostate tissue (p. 3061, col. 2). Bera et al teach that NGEP is expressed only in normal prostate and prostate cancer cells (p. 3063, col. 1).

One cannot extrapolate the disclosure of the specification to the enablement of the claims because the specification does not provide guidance or examples for detecting prostate cancer in a subject, comprising detecting expression of SEQ ID NO:2. It is clear from the art and the instant specification that SEQ ID NO:2 is not differentially expressed between normal and cancerous prostate, therefore, one of skill in the art could not distinguish normal prostate from prostate cancer based on the expression of SEQ ID NO:2. The specification provides neither guidance on nor exemplification of how to correlate the presence of SEQ ID NO:2 with the presence of prostate cancer as distinguished from the presence of normal prostate. Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker to successful clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly

applicable to other oncogenic disorders. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and **specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome**. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Given the expression of SEQ ID NO:2 is not specific to prostate cancer and cannot distinguish between normal prostate and the presence of prostate cancer, one of skill in the art could not predictably detect prostate cancer based on the expression of SEQ ID NO:2.

Therefore, in view of the state of the art, the quantity of experimentation necessary to distinguish between normal and prostate cancer, the lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

15. All other objections and rejections recited in the Office Action mailed November 29, 2006 are hereby withdrawn.

16. **Conclusion:** Claims 7-9 are allowed. Claims 1, 4-6, 10, 11, 24-30, 39, 40, and 47-53 are rejected.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642